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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/632,101	08/01/2003	Marco Ciufolini	065691-0332	1920

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FOLEY AND LARDNER LLP
SUITE 500
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WASHINGTON, DC 20007

EXAMINER

STOCKTON, LAURA LYNNE

ART UNIT	PAPER NUMBER
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1626

MAIL DATE	DELIVERY MODE
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05/18/2007

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/632,101

Applicant(s)

CIUFOLINI ET AL.

Examiner

Laura L. Stockton, Ph.D.

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
 - If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
 - If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
 - Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on February 27, 2007.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,54-76 and 78-81 is/are pending in the application.
- 4a) Of the above claim(s) 55-60 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1, 54, 61-76 and 78-81 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

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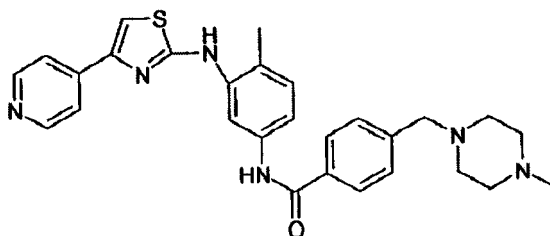
DETAILED ACTION

Claims 1, 54-76 and 78-81 are pending in the application.

Election/Restrictions

Applicant's election without traverse of modified Group II, and the species of Example 80 found on pages 64-65 of the instant specification (reproduced below), in the reply filed on July 15, 2005 was acknowledged in a previous Office Action. Modified Group II embraces wherein R⁶ represents the definition of (i), (ii) and (iii).

080: 4-(4-Methyl-piperazin-1-ylmethyl)-N-[4-methyl-3-(4-pyridin-4-yl-thiazol-2-ylamino)-phenyl]-benzamide



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The requirement was deemed proper and made FINAL in a previous Office Action.

It is noted that because of the amendments to independent claim 1, the elected species is not embraced by independent claim 1.

Subject matter not embraced by modified Group II and claims 55-60 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to nonelected inventions. Election was made **without** traverse in the reply filed on July 15, 2005.

Rejections made in the previous Office Action that do not appear below have been overcome. Therefore

arguments pertaining to these rejections will not be addressed.

Response to Amendment

The Declaration under 37 CFR 1.132 filed February 27, 2007 is insufficient to overcome the rejection of claims 1, 54, 61 and 73-76 based upon 35 USC 103 over Lago {WO 00/33842}, Dexter et al. {U.S. Pat. 3,467,666}, Spivack et al. {U.S. Pat. 3,201,409}, Illig et al. {U.S. Pat. 6,291,514}, Stieber et al. {U.S. Pat. 2003/0158199}, and Dhanoa et al. {U.S. Pat. 2001/0044545} as set forth in the last Office action because, firstly, the showing is not commensurate in scope with the instant claims. In re Greenfield, 197 U.S.P.Q. 227 (1978) and In re Lindner, 173 U.S.P.Q. 356 (1972). Also see M.P.E.P. 716.02(d).

Secondly, Applicant states (pages 10-11, paragraph 13) that the instant claimed compounds are those of Compounds 002 (page 20), 005 (page 21), 006 (page 21)

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and 088 (page 73) and have been used in the comparison, but these compounds are not embraced by the currently amended independent claim 1. Note, the amended definition of the R^1 variable substitutions in currently amended independent claim 1, particularly "a nitrogen atom".

Thirdly, Applicant states (page 9, paragraph 12) that a compound from the Illig et al. reference {U.S. Pat. 6,291,514} was not tested because the compounds are very difficult to synthesize and would require multiple steps. In response, the compounds of Illig et al. were generically embraced by the instant claimed invention. Is Applicant stating for the record that the instant claimed compounds are not enabled because the compounds of instant formula I of instant independent claim 1 cannot be made? Is Applicant stating that it is acceptable that Applicant cannot make the compounds of their invention without difficulty but it is acceptable to pass the burden onto

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one skilled in the art to make the instant claimed compounds with undue experimentation? For all the reasons given above, the Declaration under 37 CFR 1.132 filed February 27, 2007 is insufficient to overcome the rejection.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 54, 61-76 and 78-81 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s),

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at the time the application was filed, had possession of the claimed invention.

No persuasive support could be found in the specification or the originally filed claims for the expressions "at least one heteroatom selected from the group consisting of halogen or a nitrogen atom" found in claims 1 and 62-67 and "bearing a nitrogen group" in claim 69. Applicant alleges support for this expression on page 4, lines 2-3. However, such showing for these expressions is not found persuasive because these expressions are not found in either location. Again, it is suggested that the specific examples found on page 17 of the instant specification, lines 9-10, which define the expression "bearing a pendant basic nitrogen functionality", said expression is found in the originally filed claim language. Therefore, the claims lack written description as such.

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The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 54, 61-76 and 78-81 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 1, all occurrences, there is a valence problem having a "nitrogen atom" alone as a substituent {i.e., -N only}. See variables R^1 , R, R', etc. and claims 62-67, all occurrences, for same.

In claim 1, under the definition of R^1 , the "or" before "a nitrogen atom", all occurrences, should be changed to "and" for proper Markush language. See claims 62-67, all occurrences, for same.

In claim 1, under the definition of $R^6(i)$ and $R^7(i)$, the language "substituted variant thereof bearing any combination, at any one ring position of one or

more..." should be changed to "substituted by one or more...". See claim 67 for same.

In claim 1, under the definition of $R^6(i)$, "and alkoxy" should be changed to "or alkoxy". See claim 67 for same.

In claim 1, under the definition of $R^6(ii)$, $R^6(iii)$, $R^7(ii)$ and $R^7(iii)$, the phrase "which may additionally bear any combination of one or more substituents" should be changed to "which may additionally bear one or more substituents". See claim 67 for same.

In claim 1, under the definition of $R^6(iii)$ and $R^7(iii)$, an "or" should be added before "5-thiazolyl". See claim 67 for same.

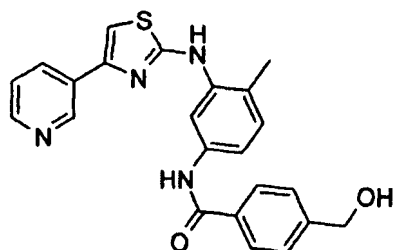
In claim 1, under the definition of $R^7(iv)$, the phrase "linear or branched alkyl group containing one or more group" is unclear as to its meaning and "group" should be plural. What is the group? Therefore, the metes and bounds of the claims cannot be ascertained.

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In claim 1, under the definition of $R^7(iv)$, the comma after "a nitrogen atom" should be deleted because it appears as if something is missing.

In claim 61, there are numerous specie listed which are not embraced by independent currently amended claim 1 because of the specific definition of heteroatom in currently amended claim 1. Further, there are numerous specie that are not embraced by claim 1 for the same as mentioned before and for other reasons. For example, a species such Compound vi listed in claim 61 (Example 030 found on page 41 of the instant specification - reproduced below), has a hydroxymethyl group substituted on the phenyl ring (represented by the variable R) but it is not found in independent claim 1 that the phenyl (represented by the R variable) is optionally substituted with a group such as a hydroxymethyl group.

030: 4-Hydroxymethyl-N-[4-methyl-3-(4-pyridin-3-yl-thiazol-2-ylamino)-phenyl]-benzamide



In reviewing the originally filed claims and the originally filed specification, a compound such as Compound vi was never embraced by the claim language. Specie in claim 61 such as Compound xv (Example 037 on page 43); Compound lxv (Example 050 on page 48); Compound xci (Example 088 on page 73); etc. also suffer the same problem. See following a few additional specie listed in claim 61 that, for one reason or another, are not embraced by independent claim 1:

- a) compound i (Example 068 on page 61);
- b) compound ii (Example 069 on page 61);
- c) compound iii (Example 070 on page 61);
- d) compound iv (Example 071 on pages 61-62);
- e) compound vi (Example 030 on page 41); etc.

In claim 62, under the definition of R, the "cycloalkyl", "aryl" or "heteroaryl" being optionally substituted with an alkyl, cycloalkyl, aryl or heteroaryl group as well as these groups further being optionally substituted lack antecedent basis from claim 1. See claims 63-67 for same.

In claim 62, at the end of the claim, the comma after "a nitrogen atom" should be deleted because it appears as if something is missing.

In claims 63-65, the formulas in each claim lacks antecedent basis from claim 1 (see the -NH-R group, -CH₂-NH-R group and O-R group, respectively, attached to the phenyl rings).

In claim 63, the R variable is defined differently than as stated in independent claim 1 (i.e., -SO₂-R"). See claims 64 and 65 for same.

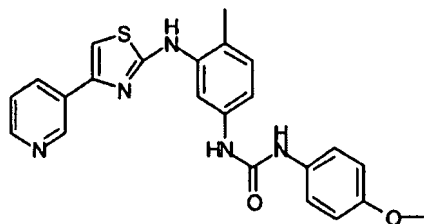
In claim 63, it is unclear if the -COR group and the -CONRR' group are defining R" or R. See claims 64 and 65 for same.

In claim 63, the R variable is being used to define itself (see last three lines of claim). See claims 64 and 65 for same.

In claim 66, at the end of the claim, the comma after "a nitrogen atom" should be deleted because it appears as if something is missing.

Claim 68 lacks antecedent basis from claim 67 and independent claim 1. See, for example, compound (i) (Example 009 on page 29 - reproduced below), which has a methoxy group substituted on the phenyl ring.

009: 1-(4-Methoxy-phenyl)-3-[4-methyl-3-(4-pyridin-3-yl-thiazol-2-ylamino)-phenyl]-urea



Claim 69 lacks antecedent basis from claim 67 and independent claim 1 since the "nitrogen group" in claim 69 is absent from claims 1 and 67.

In claim 69, an "or" should be added before structure (f).

In Claims 70-72, X representing group (d) lacks antecedent basis from claim 67.

Claims 78-81 lack antecedent basis from claim 1.

NOTE: Applicant is strongly encouraged to carefully consider the claim language compared to each and every specie found in the claims and the structure of each and every claimed specie found in the instant specification before Applicant contemplates filing any more responses.

It is also suggested that instead of, or in addition to, the specie being listed by Roman numerals in the claims (such as in Claims 61, 68, etc.), that the example numbers be added to the claims. For instance, the first compound listed in instant claim 61 is Example 068 (found on page 61 of the instant

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specification). Claim 61 can list this first species as follows:

4-Diethylaminomethyl-N-[4-methyl-3-(4-pyridin-3-yl-thiazol-2-ylamino)-phenyl]-benzamide (Example 068);

or

(i) 4-Diethylaminomethyl-N-[4-methyl-3-(4-pyridin-3-yl-thiazol-2-ylamino)-phenyl]-benzamide (Example 068);

as well as the remaining specie in the same format.

Response to Arguments

Applicant's arguments filed February 27, 2007 have been fully considered. Applicant states that all of the compounds are embraced by currently amended independent claim 1. In response, since the specific definitions of heteroatom have been added to the claims, there are numerous specie not embraced by currently amended claim 1.

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Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1, 54, 61-76 and 78-81 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-22 of copending Application No. 10/523,018 and over claims 31 and 32 of copending Application No. 10/567,557. Although the conflicting claims are not identical, they are not patentably

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distinct from each other because the instant claimed compounds are generically described in 10/523,018.

Note claim 1 in instant application and in copending Application No. 10/523,018. Note claim 31 in copending Application No. 10/567,557 as well as the compounds and formulas on pages 7-25 of the specification in copending Application No. 10/567,557.

The indiscriminate selection of "some" among "many" is *prima facie* obvious, In re Lemin, 141 USPQ 814 (1964). The motivation to make the claimed compounds derives from the expectation that structurally similar compounds would possess similar activity (e.g., c-kit inhibitors). One skilled in the art would thus be motivated to prepare products embraced by the copending applications to arrive at the instant claimed products with the expectation of obtaining additional beneficial products which would be c-kit inhibitors. The instant claimed invention would have been suggested and therefore, obvious to one skilled in the art.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Response to Arguments

Applicants' arguments filed February 27, 2007 have been fully considered. Applicants state that since the rejection is provisional, Applicants will address the rejection if it ever becomes a non-provisional rejection.

Since Applicant has amended independent claim 1, and other dependent claims, by limiting the definition of heteroatom, the rejection of the claims over Lago {WO 00/33842} and Stieber et al. {U.S. Pat. 2003/0158199} under 35 USC § 103 has been withdrawn.

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Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1, 54, 61 and 73-76 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dexter et al. {U.S. Pat. 3,467,666}, Spivack et al. {U.S. Pat. 3,201,409}, Illig et al. {U.S. Pat. 6,291,514} and Dhanoa et al. {U.S. Pat. 2001/0044545}, each taken alone or in combination with each other when similar activities are asserted.

Determination of the scope and content of the prior art (MPEP §2141.01)

Applicants claim substituted phenylamino-2-thiazole compounds. **Dexter et al.** (columns 1-2; column 3, lines 35-38; and especially the compound of Example 13 in column 9), **Spivack et al.** (column 1; and especially the

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compound of Example 19 in column 9), **Illig et al.**

(columns 4-5; Formula IV in column 17; columns 24-27; and especially the compound in column 18, lines 25-26), and **Dhanoa et al.** (page 3; Formula III on page 4; the compositions on pages 8-9; and especially compound 24 on page 6, paragraph [0120]) each teach substituted phenylamino-2-thiazole compounds that are structurally similar to the instant claimed compounds.

Ascertainment of the difference between the prior art and the claims

(MPEP §2141.02)

The difference between the compounds of Illig et al. and Dhanoa et al. and the instant claimed compounds is that the instant claimed compounds are generically described in the prior art.

The difference between the compounds of Dexter et al. and Spivack et al. and the compounds instantly claimed is that of a hydrogen versus a methyl on a phenyl ring (see the instant R⁴ variable definition).

***Finding of prima facie obviousness--rational and motivation (MPEP
§2142-2413)***

The indiscriminate selection of "some" among "many" is *prima facie* obvious, In re Lemin, 141 USPQ 814 (1964). The motivation to make the claimed compounds derives from the expectation that structurally similar compounds would possess similar activity (e.g., antagonizing the myt1 kinase receptor).

Further, it is well established that the substitution of methyl for hydrogen on a known compound is not a patentable modification absent unexpected or unobvious results. In re Wood, 199 U.S.P.Q. 137 (C.C.P.A. 1978) and In re Lohr, 137 U.S.P.Q. 548, 549 (C.C.P.A. 1963). The motivation to make the claimed compounds derives from the expectation that structurally similar compounds would possess similar activity (e.g., a muscle relaxant).

One skilled in the art would thus be motivated to prepare products embraced by the prior art to arrive at the instant claimed products with the expectation of

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obtaining additional beneficial products which would, for example, antagonize the myt1 kinase receptor. The instant claimed invention would have been suggested and therefore, obvious to one skilled in the art. A strong case of *prima facie* obviousness has been established.

Response to Arguments

Applicant's arguments filed February 27, 2007 have been fully considered. Applicants argue that: (1) a *prima facie* case of obviousness has not been established; (2) there is no teaching or suggestion in the art to modify the references; (3) the instant claimed compounds are unexpected properties as demonstrated in the Declaration under 37 CFR 1.132 filed February 27, 2007; and (4) nothing in the prior art would suggest that the claimed compounds would possess the selective inhibition of c-kit.

All of Applicant's arguments have been considered but have not been found persuasive. It is disagreed

that a *prima facie* case of obviousness has not been established. The cited prior art references do provide motivation to prepare the instant claimed compounds as discussed above in the rejection. It would appear that Applicant is arguing that if a rejection under 35 USC § 102 can not be made, than a rejection under 35 USC § 103 should not be made. However, this is not one of the factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a).

Additionally, there is no requirement that the prior art must suggest that the claimed product will have the same or similar utility as that discovered by applicant in order to support a legal conclusion of obviousness. *In re Dillon*, 16 U.S.P.Q. 2d 1897, 1904 (Fed. Cir. 1990). However, some of the cited prior art teach that their compounds have at least one or more of the same utilities that Applicant has disclosed in the

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instant specification. Illig et al. (column 3, lines 54-58) teach treating psoriasis and the instant specification discloses that psoriasis can be treated by administering the instant claimed compounds (page 91, line 17). Dhanoa et al. (page 2, paragraph [0026]) teach treating diabetic complications and the instant specification discloses that diabetes mellitus and its chronic complications can be treated by administering the instant claimed compounds (page 91, line 6). A compound and its properties are inseparable. In re Papesch, 137 USPQ 43 (CCPA 1963). The Declaration under 37 CFR 1.132 filed February 27, 2007 was found insufficient for reasons stated above. For all the reasons given above, the rejection is maintained.

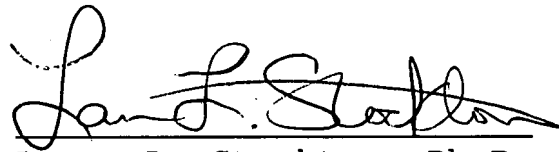
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Laura L. Stockton whose telephone number is (571) 272-0710. The examiner can normally be reached on Monday-Friday from 6:15 am to 2:45 pm. If the

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examiner is out of the Office, the examiner's supervisor, Joseph McKane, can be reached on (571) 272-0699.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

The Official fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

A handwritten signature in black ink, appearing to read "Laura L. Stockton", written over a horizontal line.

Laura L. Stockton, Ph.D.
Patent Examiner
Art Unit 1626, Group 1620
Technology Center 1600

May 16, 2007